I hereby certify that this paper (along with any paper referred to as being attached or enclosed) is being deposited with the United States Postal Service on the date shown below with sufficient postage as first class mail in an envelope addressed to the: Mail Stop Missing Parts, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450.

| | Sushma S. Brady |
|--------------------------------|---|
| | (Type or print name of person mailing paper) |
| Date: July 16, 2004 | Rulina & Brady |
| | (\$fgnature of person mailing paper) |
| IN THE UNITED STATES PA | TENT AND TRADEMARK OFFICE |
| In re PATENT APPLICATION of |) Group Art Unit:) Attorney Docket No. 249.P2 |
| Becker et al. |) Examiner: Louise N. Leary |
| Serial No: 10/785,497 |) |
| Filed: February 24, 2004 |) |
| Title: PRODRUGS OF PHOSPHONATE |)) |
| NUCLEOTIDE ANALOGUES AND |) |
| METHODS FOR SELECTING AND | |
| MAKING SAME | |

PRELIMINARY AMENDMENT AND CORRECTION OF INFORMALITIES

Mail Stop Missing Parts Commissioner for Patents P.O. Box 1450 Alexandria, VA 22313-1450

Dear Sir:

This is in response to the "Notice to File Corrected Application Papers" mailed May 17, 2004, with a response date of July 17, 2004. Applicants respectfully submit a substitute specification to correct informalities.

SUBSTITUTE SPECIFICATION

Prior to examination on the merits, please replace the specification with the enclosed substitute specification herein according to 37 CFR 1.52, 1.121(b)(3) and 1.125.

The substitute specification is submitted in clean and marked up format in accordance with 37 CFR 1.125. The changes made in the substitute specification are as follows:

On specification page 4, line 10, please amend structure (3) as follows

B-E-OCH₂
$$\mathbb{P}^{1}$$
_{||R}¹
 \mathbb{R}^{2} (3)

On specification page 4, line 16, please amend structure (4) as follows

B-E-OCH₂-P
$$\stackrel{\text{O}}{=}$$
 R1

On specification page 7, line 29, correct the structure A-OH₂P(O)(OH)₂ to read A-OCH₂P(O)(OH)₂.

On specification page 7, last line, please amend the structure as follows

Amend the specification to move embedded drawings to separate figures and insert a description of the drawings.

Amend the claims to reflect the subject matter now claimed as noted below: